B1 positions numbered 95 and 96 and 328 and 329 in the human RI sequence as numbered in Lee et al. are all cysteines. It was theorized that these cysteine residues would be the most likely to be oxidized to form disulfide bonds which would interfere with the biological activity of the molecule. Note that in SEQ ID NO:2 below, these cysteine residues appear as amino acids 96, 97, 329 and 330, the difference being the N-terminal methionine which is counted as residue 1 in the deduced sequence of SEQ ID:2 below and as residue 0 in the sequence of Lee et al. To remain consistent with prior work in the field, the numbering convention used by Lee et al. is used in this specification.

Cont 1

Please insert the following new paragraph for the paragraph which previously started on page 7, line 23 to page 7, line 36.

B2 As will be discussed with the experimental results below, it was found possible to inhibit the formation of disulfide bonds between adjacent cysteine residues of a ribonuclease inhibitor by replacing the adjacent cysteine residues with alanine residues. The mutant human pancreatic ribonuclease inhibitor molecules thus created, have pairs of alanine-for-cysteine substitutions at both amino acids 94 and 95, at both amino acid positions 328 and 329, or substitutions for all four of the cysteine residues. It was demonstrated that the replacing of any or all of the cysteine residues with alanine did not markedly impair the ability of the human ribonuclease inhibitor to bind RNase A. There was, however, some slight diminution in affinity to ribonuclease for some of the variants.

In the Claims:

Please amend Claims 1 and 9 as follows and add the following new Claim 15:

B3 1. A mutant ribonuclease inhibitor having at least one amino acid substitution in at least one of two adjacent cysteine residues present in the amino acid sequence of the wild-type ribonuclease inhibitor, the substitution being to an amino acid residue not capable of forming a disulfide bond with an adjacent residue, the mutant ribonuclease inhibitor having a greater resistance to oxidation, the mutant ribonuclease inhibitor retaining its specificity and binding affinity to ribonuclease.